Immune-haemolytic anaemia: An unusual etiology

Lasika RADR, Lekamwasam JDVC, Mohotti M

Teaching Hospital, Karapitiya, Galle, Sri Lanka.

Correspondence: Dr. R.A.D.R. Lasika
Teaching Hospital Karapitiya, Galle, Sri Lanka.
e-mail: rukshanilasika@yahoo.com

Case report

A previously healthy, 70-year-old woman was admitted to our medical unit with the complaints of gradual onset shortness of breath after moderate exertion and fatigability for one week duration. She had been well with good exercise tolerance until about one week before admission. She did not give a history of blood loss, jaundice or change of urine color. Her dietary history was satisfactory and the systemic inquiry did not reveal any significant findings. She had no past medical history of note and particularly not used tobacco, alcohol, herbal supplements or exposed to medications or toxins. There was no family history of similar diseases.

On admission to ETU she was severely pale and mildly icteric. There was no clubbing or lymphadenopathy. Her temperature was 98.6^0 F, respiratory rate was 8 breaths per minute and oxygen saturation 99% while breathing ambient air. Lungs were clear and the abdomen was soft without organomegaly. Auscultation of the heart was normal without extraneous sounds. The remainder of the examination was normal.

Laboratory tests revealed White cell count of 20,400/mm^3 with 45% lymphocytes, 6% monocytes, and 49% neutrophils. Rest of the blood count showed haemoglobin; 3.4 g/dL, haematocrit; 11%, MCV; 106 fL, MCH; 36pg, RDW-CV; 29% and platelet count of 268,000/mm^3. Smear showed the presence of spherocytes suggestive of either an autoimmune haemolytic anaemia or spherocytic haemolytic anaemia.

The *reticulocyte* count was 13% (Reticulocyte index 2.8%) while in the direct Coombs test IgG was positive and IgM was negative. Liver function tests showed a total serum bilirubin of 69.2 umol/l with an indirect fraction of 56.2 umol/l and normal liver transaminases. Urine urobilinogen was raised and urine hemosiderin was not detected. Donath-Landsteiner test was negative.

ESR was 65 mm 1st hr and CRP was 45 mg/dL. Anti nuclear antibody test and mycoplasma antibody were negative. Clinical findings and laboratory tests were consistent with an acute haemolysis and a working diagnosis of Warm type auto immune haemolytic anaemia was made.

Further investigations were carried out to identify the etiology of autoimmune haemolytic anaemia. The appearance of bone marrow was compatible with acute haemolysis with no evidence of concomitant lymphoma. Chest radiograph showed a homogeneous opacification in the left lower zone (Figure).

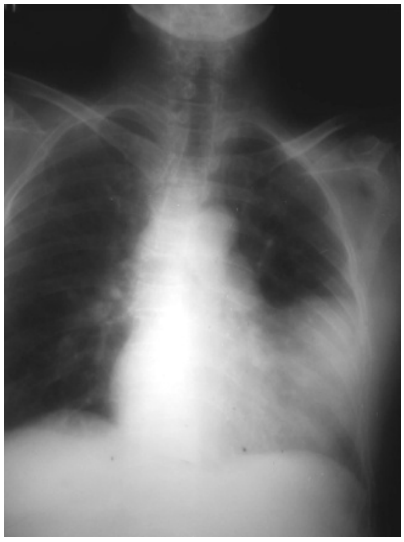

Figure: Chest radiograph showing a homogeneous opacification in the left lower zone

Ultrasonography of thorax revealed a well-defined mass measuring 7x5 cm extending laterally to the chest wall pleura and medially up to the left ventricle. CT scan thorax showed Stage $T_3N_0M_0$ malignant neoplasm in the left lingular lobe. Ultrasound guided biopsy confirmed the diagnosis of small cell carcinoma of the lung. In the absence of other causes, auto-immune haemolytic anaemia in this patient was attributed to the small cell carcinoma of the lung.

Her severe symptomatic anaemia necessitated blood transfusions. In order to eliminate the etiology patient was referred to oncologist for chemotherapy. Oral steroids was started initially for autoimmune haemolytic anaemia but later it was tailed-off while continuing the specific chemotherapy targeted for the malignancy (3). A year later she was found to be in remission of haemolytic anaemia after the successful treatment for small cell carcinoma of the lung. She did not need further blood transfusions.

Discussion

Autoimmune haemolytic anaemia (AIHA) is associated with auto-antibodies**.** The clinical manifestations of AIHA, depend greatly on the type of antibody that is produced by the abnormal immune reaction. Warm AIHA is commonly mediated through IgG auto-antibodies while the Cold AIHA is mediated through C3 component of the complements that binds the red blood cells coated with IgM antibodies.

While AIHA is commonly associated with hematological malignancies, it is an uncommon but well-described complication of solid malignancies (1-3). It is usually a late complication of malignancy and very rarely the presenting feature (2,3). Our patient's presenting features were related to haemolytic anaemia and she had no clinical features that could be attributed to the underlying lung carcinoma at the time of presentation.

Medline search revealed 53 cases of solid organ malignancies associated with AIHA reported between 1945 - 2009 (1). Of those, 9 cases were lung carcinomas and all the 9 cases were non-small cell carcinomas (1,4).

This is an unusual case of small cell carcinoma of lung presenting as haemolytic anaemia. We suggest that the search for underlying malignancies should be extended to the lungs in order to not to miss out lung malignancies. Our patient was referred for chemotherapy and after completing the chemotherapy, in one-year follow up she was found to be Coombs test negative and there was no evidence of ongoing haemolysis. Thus the casual link between the haemolytic anaemia and underlying malignancy was supported by the dramatic resolution of haemolysis after initiation of lung cancer directed treatment.

Therefore when a patient presents with haemolytic anaemia the search for underlying malignancies should be extensive and include solid malignancies as well.

References

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